BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

Practitioner's Docket No. U 014801-0 *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Manne Satyanarayana REDDY, et al.
Serial No.: 10/653,694 Group No.: 1615
Filed: September 2, 2003 Examiner:
For: PROCESS FOR PREPARATION OF CRYSTALLINE FORM-1 OF PANTOPRAZOLE SODIUM SESQUIHYDRATE

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF CERTIFIED COPY

Attached please find the certified copy of the foreign application from which priority is claimed for this case:

Country: INDIA

Application Number: 648/MAS/2002

Filing Date: SEPTEMBER 2, 2002

WARNING: "When a document that is required by statute to be certified must be filed, a copy, including a photocopy or facsimile transmission of the certification is not acceptable." 37 C.F.R. 1.4(f) (emphasis added).

CERTIFICATE OF MAILING (37 C.F.R. 1.8a)

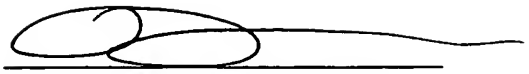
I hereby certify that this correspondence is, on the date shown below, being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

Signature

Date: MAY 28, 2004

JANET I. CORD

(type or print name of person certifying)



SIGNATURE OF PRACTITIONER

Reg. No. 33778

JANET I. CORD
(type or print name of practitioner)

Tel. No.: (212) 708-1935

P.O. Address

Customer No.: 00140

c/o Ladas & Parry LLP
26 West 61st Street
New York, N.Y. 10023

NOTE: "The claim to priority need be in no special form and may be made by the attorney or agent, if the foreign application is referred to in the oath or declaration, as required by § 1.63." 37 C.F.R. 1.55(a).

THE PATENTS ACT, 1970

It is hereby certified that annexed hereto is a true copy of Application, Complete Specification, Abstract & Drawings of the extract of Patent Application No.648/MAS/2002, dated 02/09/2002 by Dr. Reddy's Laboratories Limited, having its registered office at 7-1-27, Ameerpet, Hyderabad 500 016, Andhra Pradesh, India.

.....

.....**In witness thereof**

I have hereunto set my hand

Dated this the 20th day of May 2004

M. S. Venkataraman

(M.S. VENKATARAMAN)
ASSISTANT CONTROLLER OF PATENTS & DESIGNS

PATENT OFFICE BRANCH
GOVERNMENT OF INDIA
Guna Complex, 6th Floor, Annex.II
No.443, Anna Salai, Teynampet, Chennai – 600 018

Received Rs 5000 in ~~Cash~~
Cheque ~~/M.O./P.O./D.D.~~/on 02.09
Vide C.B.R. No. 4554 16 ... 02
21/9/...

FORM 1

THE PATENTS ACT, 1970
APPLICATION FOR GRANT OF A PATENT (Section 5(2), 7and Rule 33A)

We, Dr. Reddy's Laboratories Limited, an Indian company having its registered office at 7-1-27, Ameerpet, Hyderabad, Andhra Pradesh, INDIA, 500 016 hereby declare

1. (a) that we are in possession of an invention titled "**An Improved process for preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate**".
   (b) that the complete specification relating to this invention is filed with this application.
   (c) that there is no lawful ground of objection to the grant of a patent to us.
2. further declare that the inventors for the said invention are **Manne Satyanarayana Reddy, Sajja Eswaraiah, Vijayavitthal Thippannachar Mathad, Govindan Shanmugam, Pondichetty Anilkumar and Elati Ravi Ram Chandrashekar.** All citizens & residents of India belonging to **Dr. Reddy's Laboratories Limited, 7-1-27, Ameerpet, Hyderabad – 500 016, Andhra Pradesh.**
3. that we are the assignee of the true and first inventors
4. that our address for service in India is as follows;

Dr. Manne Satyanarayana Reddy,
Vice President-R&D
Dr. Reddy's Laboratories Limited
7-1-27, Ameerpet
Hyderabad, A.P., 500 016

5. following declaration was given by inventors.
We, the true and first inventors for this invention declare that the applicant Herein is our assignee.

Signed)__________
Manne Satyanarayana Reddy,
H.No. 8-3-167/D/16,
Kalyan Nagar,
Near AG Colony,
Erragadda,
Hyderabad-500 038.

Signed)__________
Sajja Eswaraiah,
LIG 100,
Dharma Reddy Colony,
K.P.H.B Colony
Kukatpally,
Hyderabad - 500 072.

Signed)_____

Vijayavitthal Thippannachar Mathad,
Flat No: 114, Adithya homes,
Adithya Nagar, opp. JNTU,
Pragathi Nagar Road,
Kukatpally,
Hyderabad-500 072.

Signed)_____

Govindan Shanmugam,
HIG-64, Bharat Nagar Colony,
Hyderabad-500 018

Signed)_____

Pondichetty Anilkumar,
H. No: 9-76/3/A,
Madhura Nagar Colony,
Risala Bazar,
Secunderabad-500 010.

Signed)_____

Elati Ravi Ram Chandrashekar,
H. No: ER-5,
Jalavayu Vihar,
Opp: K.P.H.B Colony,
Hyderabad-500 072.

6. that to the best of our knowledge, information and belief, the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application

7. following are the attachments with the application
   (a) complete specification (---15 pages, in triplicate)
   (b) abstract of the invention (--01-- page, in triplicate)
   (c) drawings (---02- pages, in triplicate)
   (d) fee Rs. 5000.00 (five thousand rupees only) in A/C Payee Cheque vide No. "336410" dated August 28th drawn on HDFC Bank Limited, Lakdikapool, Hyderabad-500 004.

We request that a patent may be granted to us for the said invention

Dated this 30th day of August 2002. (Signed)

Dr. Manne Satyanarayana Reddy,
Vice President-R&D
Dr. Reddy's Laboratories Limited.

To, The Controller of Patents
The Patents Office Branch, Chennai.

FORM-2

THE PATENTS ACT, 1970

COMPLETE SPECIFICATION

(SECTION 10)

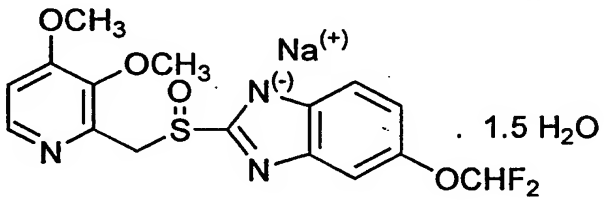
An improved process for preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate

Dr. Reddy's Laboratories Limited,
An Indian Company having its registered office at
7-1-27, Ameerpet,
Hyderabad-500 016, A.P., India.

The following specification particularly describes the nature of this invention and the manner on which it is to be performed.

FIELD OF THE INVENTION:

The present invention relates to an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate, chemically known as 5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl) methyl] sulfinyl]-1H-benzimidazole sodium sesquihydrate. The Pantoprazole sodium sesquihydrate of the present invention can be depicted as Formula (1).



Formula (1)

BACK GROUND OF THE INVENTION:

Pantoprazole sodium sesquihydrate is a known Anti-ulcerative drug, gastric acid secretion inhibitor and has been used for the treatment of ulcer patients.

USP 4,758,579 specifically claimed the Pantoprazole and its pharmaceutically acceptable salts. The patent also described the process for the preparation of pantoprazole and its related compounds.

The process for the preparation of pantoprazole sodium sesquihydrate is not described specifically in '579 patent, but disclosed in the summary of the invention that "the salts are obtained by dissolving free base in a suitable solvent, for example in a suitable halo hydrocarbon solvent such as methylene chloride or chloroform or a low molecular weight aliphatic alcohol such as ethanol or iso propanol or a ketone like acetone or water, which contains the desired acid or base, or to which the desired acid or base is added (if

necessary) in the precisely calculated stochiometric amount accompanied by filtering, evaporating the solvent yielded the corresponding salt of Pantoprazole.

The process disclosed in the above '579 patent suffers from the draw back that more number of stages and high volume of solvents are involved in the salt preparation.

J.Med.Chem. 35, 1049-1057 (1992) described the process for the preparation of Pantoprazole sodium sesquihydrate, which comprises the dissolution of pantoprazole freebase in a mixture of ethanol and dichloromethane followed by addition of stoichiometric amount of sodium hydroxide solution and further reaction work up resulted the Pantoprazole sodium sesquihydrate with a melting point of 130^{o}C.

The process of said journal also suffers from the draw back of using mixture of solvents in a high volume, which in turn the desired product was not isolated, hence the volume of ethanol was reduced to isolate the product.

The crystalline forms of Pantaprazole sodium sesquihydrate were not reported in any of the relevant references known in the art till date.

The inventors of the present invention have prepared the crystalline form of pantoprazole sodium sesquihydrate according to the process disclosed in **J.Med.Chem. 35, 1049-1057 (1992)** with less volume of ethanol and analyzed the crystalline structure by X-ray diffractogram and hereinafter it is referred as prior art crystalline Form-I of Pantoprazole sodium sesqui hydrate for convenience.

Many attempts have been done to provide the novel crystalline form of Pantaprazole sodium sesquihydrate but in all the cases the crystalline structure of product is substantially similar to that of prior art crystalline Form-I of Pantoprazole sodium sesqui hydrate.

Since polymorphic forms of drug substances are known to differ in their physical properties such as melting point, solubility, chemical reactivity etc., they can appreciably influence the pharmaceutical properties such as dissolution rate and bioavailability and Pentaprazole sodium sesqui hydrate is being a known anti ulcerative drug, it is important to further evaluate the polymorphism to obtain newer polymorphs or to provide an alternate process in a cost-effective, non-hazardous and commercially viable for existing polymorphs.

The main aspect of the present invention is to provide an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate. The improved process of the present invention is simple, cost effective, non-hazardous and industrially scalable.

The crystalline nature of the pantoprazole sodium sesquihydrate of the present invention has been analyzed by XRD and found that the crystalline structure is identical to that of prior art crystalline Form-I of Pantoprazole sodium sesqui hydrate.

SUMMARY OF THE INVENTION:

The present invention is related to an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate.

The process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate comprises dissolution of Pantoprazole free base in which it substantially dissolves at an ambient temperature containing a stoichiometric quantity of sodium hydroxide, filtration of the clear solution and followed by addition of anti-solvent in which the product is insoluble to isolate the desired crystalline compound. The solvents for dissolution are selected from C1-C4 straight or branched chain alcohols,

tetrahydrofuran, ethyl acetate and the solvents for isolation are selected from a group of aliphatic or alicyclic hydrocarbon solvents, such as petroleum ether, hexane, n-heptane, cyclohexane, cycloheptane or chlorinated solvents such as dichloromethane or chloroform or ethereal solvents, such as diisopropyl ether or methyl-tertiary butyl ether.

BRIEF DESCRIPTION OF THE ACCOMPANYING DRAWING:

Fig.1 is characteristic XRD of prior art crystalline Form-I of Pantoprazole sodium sesquihydrate.

Fig. 2 is characteristic XRD of crystalline Form-I of Pantoprazole sodium sesquihydrate obtained as per the process of the present invention.

DETAILED DESCRIPTION OF THE INVENTION:

The present invention relates to an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate.

The crystalline Form-I of Pantoprazole sodium sesquihydrate of the present invention is characterized by X-ray Powder diffractogram, Differential Scanning Colorimetry thermogram and Infra red spectra.

The X-ray powder diffractogram of the crystalline Form-I of pantoprazole sodium sesquihydrate of the present invention and the prior art crystalline Form-I of Pantoprazole sodium sesqui hydrate are measured on a Bruker Axs, D8 Advance Powder X-ray Diffractometer with Cu K alpha-1 Radiation source. The pattern of X-ray diffractogram of these two compounds is found to be identical.

The X-ray powder diffractogram of prior art crystalline Form-I of Pantoprazole sodium sesqui hydrate is substantially as depicted in Figure (1).

The X-ray powder diffractogram of the crystalline Form-I of pantoprazole sodium sesquihydrate obtained in the present inventive process is substantially as depicted in Figure (2).

The characteristic peaks (in 2-theta values) and their relative intensities (in percentage) of crystalline Form-I of pantoprazole sodium sesquihydrate are shown in the following table (1).

Table-1:

Prior art crystalline Form-I of Pantoprazole sodium sesquihydrate		**Crystalline Form-I of Pantoprazole sodium sesquihydrate obtained in the present process**	
2θ(°)	**Intensity (%)**	**2θ(°)**	**Intensity (%)**
5.238	100	5.326	100
20.486	7.6	20.581	13.0
22.148	6.2	22.254	10.5
16.653	4.2	16.687	6.7
13.3	3.3	16.836	6.0
19.97	3.3	14.543	5.3
24.497	3.1	20.061	4.9
14.459	2.9	13.366	4.8
22.812	2.9	24.587	4.8
13.024	2.8	13.102	4.5
26.278	2.7	26.353	4.5
27.798	2.7	7.385	4.2
7.294	2.7	22.886	4.0
27.037	2.5	24.122	3.7
24.002	2.4	17.62	3.2
25.32	2.3	27.887	3.1
17.527	2.2	11.531	2.8

37.572	2.0	27.147	2.7
11.428	1.7	37.642	2.5
28.737	1.7	25.405	2.4
29.383	1.6	29.487	2.4
17.884	1.5	16.207	1.7
32.652	1.4	17.966	1.6
24.957	1.3	18.498	1.5
10.523	1.1	15.92	1.4
30.861	1.1	25.026	1.4
34.671	1.1	34.748	1.3
15.844	1	26.803	1.2
18.404	1	21.271	1.2
21.214	1	33.694	1.1
23.26	1	12.472	1
33.647	1	15.317	1
12.345	0.9	23.33	1
16.15	0.8	31.878	1
15.207	0.7	28.842	1.9
30.18	0.6	21.621	0.9
------	-----	30.926	0.9
------	------	10.63	0.8
------	------	9.868	0.6

The crystalline Form-I of pantoprazole sodium sesquihydrate of the present invention is also characterized by Differential scanning calorimetry. The Differential scanning calorimetry thermogram exhibits a significant endo peak around 136 ^{O}C.

The crystalline Form-I of pantoprazole sodium sesquihydrate of the present invention is further characterized by Infrared spectrum, which is measured by KBr-transmission method.

The identified significant IR bands are observed around 456, 477, 500.7, 532.3, 575.2, 397.3, 643.9, 685.6, 719.8, 764.4, 804.3, 860.4, 909.1, 922.8, 986.6, 1028.1, 1065.0, 1087.7, 1113.0, 1139.9, 1171.5, 1293.0, 1319.6, 1365.3, 1383.7, 1401.3, 1467.9, 1490.3, 1572.3, 2059.8, 2600.5, 2639.0, 2666.5, 2697.2, 2741.5, 2794.9, 2867.9, 3030.0, 3061.0, 3290.6.

Another aspect of the present invention is to provide an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate.

Accordingly, an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate, which comprises;

i. dissolving Pantoprazole free base in a solvent in which it dissolves at a temperature of 25-50^{O}C containing the stoichiometric amount of aqueous sodium hydroxide solution or by adding if necessary;

ii. optionally filtering the clear solution obtained in step (i);

iii. adding the solvent in which the Pantoprazole sodium is insoluble, accompanied by optionally cooling the mass to –10 to +20^{O}C and accompanied by stirring till the compound substantially crystallizes;

iv. filtering the crystallized solid in step (iii) by conventional methods;

v. drying of the solid obtained in step (iv) at a temperature of 40-90°C, preferably 40-50^{O}C under vacuum to a constant weight to afford the desired crystalline Form-I of Pantoprazole sodium sesqui hydrate.

The solvents for dissolving Pantoprazole freebase are selected from the group comprising of C1-C4 straight or branched alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, secondary butanol or tertiary butanol or other solvents such as tetrahydrofuran or acetonitrile or ethylacetate containing stoichiometric amount of aqueous sodium hydroxide solution. The preferred solvent for dissolution is tetrahydrofuran, acetonitrile or ethyl acetate.

The solvents for isolating the desired crystalline Form-I of Pantoprazole sodium sesqui hydrate as an anti solvent are selected from a group of aliphatic or alicyclic hydrocarbon solvents comprising of petroleum ether, hexane, n-heptane, cyclohexane or cyclo heptane, or chlorinated solvents such as dichloromethane or chloroform or ethers having C1-C4 carbon atoms in straight or branched chain such as dimethyl ether, diethyl ether, di isopropyl ether, di butyl ether or methyl tertiary butyl ether . The preferred anti solvents are dichloromethane or diisopropylether or methyl-tertiary butyl ether.

The inventors of the present invention were prepared the desired crystalline Form-I of Pantoprazole sodium sesquihydrate from various solvents and analyzed the crystalline structure by X-ray diffractogram, which are substantially identical. The laboratory findings are tabulated in the following table (2).

Table-2

Pantoprazole free base (in grams)	Dissolution solvent /volume (in ml)	Anti Solvent/ Volume (in ml)	Yield (in grams)	Moisture content (%)	XRD
75	Tetrahydrofuran / 525	Methyl tertiary butyl ether/675	74.6	6.43	Form-I
25	Tetrahydrofuran / 200	Isopropyl ether/225	22.2	6.45	Form-I
25	Isopropylalcohol / 200	Isopropyl ether/225	23.4	6.86	Form-I
25	Acetonitrile / 200	Methyl tertiary butyl ether /225	24.5	6.38	Form-I
25	Acetonitrile / 200	Dichloromethane /225	21.4	6.88	Form-I
25	Methanol / 25	Methyl tertiary butyl ether/550	16.4	6.4	Form-I
25	n-Propanol / 25	Methyl tertiary butyl ether/300	16.8	6.30	Form-I
10	2-Butanol / 20	Methyl tertiary butyl ether / 200	7.2	6.76	Form-I

The crystalline Form-I of pantoprazole sodium sesquihydrate obtained as per the above processes is observed as free flowing, non-solvated crystalline solid which is well suited for pharmaceutical applications.

The process of the present invention is simple, non-hazardous and well suited for commercial production.

It is noteworthy to mention that the Pantoprazole free base used as the starting material for the present invention is prepared as per the process disclosed in USP '579.

The following examples illustrate the invention but don not limit the scope of further invention.

Preparation of Crystalline Form-I of Pantoprazole sodium sesquihydrate:

EXAMPLE-1:

To a stirred solution of tetrahydrofuran (350 ml), aqueous sodium hydroxide solution (5.4 grams dissolved in 10 ml of water), Pantoprazole free base (50 grams) was added and stirred at a temperature of 25-35 °C till the clear solution results. The reaction solution was filtered through hyflow and washed the bed with tetrahydrofuran (2x25 ml). Dichloromethane (400 ml) was added slowly to the filtrate in over a period of 1 hour and stirred for 5-6 hours to separate the solid mass. The separated solid mass was cooled to a temperature of 5-10 °C and further stirred for 2-3 hours. The solid was filtered, washed with dichloromethane (2x25 ml) and suck dried under vacuum. The wet solid is suspended in dichloromethane (250 ml) and stirred for 15-30 minutes. Then the solid was filtered and suck dried under vacuum and further dried at a temperature of 40-50°C to obtain crystalline Form-I of Pantoprazole sodium sesquihydrate.

(Weight: 50.4 grams, MC: 6.49% w/w)

EXAMPLE-2:

Pantoprazole free base (25 grams) was added to the stirred mixture of acetonitrile (175 ml), aqueous sodium hydroxide solution (2.7 grams in 5 ml of water) and stirred at a temperature of 25-35 °C till the clear solution results. The reaction solution was filtered through hyflow and washed the bed with acetonitrile (25 ml). Isopropyl ether (225 ml) was added slowly to the filtrate in over a period of 1/2 hour and stirred for 1-2 hours to separate the solid mass. The separated solid mass was cooled to a temperature of 5-10 °C and further stirred for 3-4 hours. The solid was filtered, washed with Isopropyl ether (25 ml) and suck dried under vacuum.

The wet solid is further dried at a temperature of 40-50^{O}C to obtain crystalline Form-I of Pantoprazole sodium sesquihydrate.

(Weight: 25.4 grams, MC: 6.55% w/w)

EXAMPLE-3:

Pantoprazole freebase (25 grams) was added to the stirred mixture of ethyl acetate (50 ml), aqueous sodium hydroxide solution (2.7 grams in 5 ml of water) and stirred at a temperature of 40-50 $^{\circ}$ C till the clear solution results. Methyl tertiary butyl ether (250 ml) was added and stirred for 3-4 hours to separate the solid mass. The separated solid mass was filtered, washed with methyl tertiary butyl ether (50 ml) and suck dried under vacuum. The wet solid is further dried at a temperature of 40-50^{O}C to obtain crystalline Form-I of Pantoprazole sodium sesquihydrate.

(Weight: 15.6 grams, MC: 7.07% w/w)

DETAILED DESCRIPTION OF THE ACCOMPANYING DRAWINGS:

Fig-1. is characteristic X-ray powder diffraction pattern of crystalline Form-I of Pantoprazole sodium sesquihydrate (according to process disclosed in J.Med.Chem.,1992,35,1049-1057).

Vertical axis: Intensity (CPS); Horizontal axis; Two Theta (degrees).

The significant two-theta values obtained are 5.238, 7.294, 10.523, 11.428, 12.345, 13.024, 13.30, 14.459, 15.207, 15.844, 16.15, 16.653, 17.527, 17.884, 18.404, 19.97, 20.486, 21.214, 22.148, 22.812, 23.26, 24.002, 24.497, 24.957, 25.32, 26.278, 27.037, 27.798, 28.737, 28.383, 30.18, 30.861, 32.652, 33.647, 34.671 and 37.572 degrees two-theta.

Fig-2. is characteristic X-ray powder diffraction pattern of crystalline form-I of Pantoprazole sodium sesquihydrate.

Vertical axis: Intensity (CPS); Horizontal axis: 2 Theta (degrees).

The significant two-theta values obtained are 5.326, 7.385, 9.868,10.63, 11.531, 12.472, 13.102, 13.366, 14.543, 15.317, 15.92, 16.207, 16.687, 16.836, 17.62, 17.966, 18.498, 20.061, 20.581, 21.271, 21.621, 22.254, 22.886, 23.33, 24.122, 24.587, 25.026, 25.405, 26.353, 26.803, 27.147, 27.887, 28.842, 29.487, 30.926, 31.878, 32.708, 33.694, 34.748 and 37.642 degrees two-theta.

We claim:

1. An improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate comprises of:
    i. dissolving Pantoprazole free base in a solvent in which it dissolves at a temperature of 25-50^{O}C containing the stoichiometric amount of aqueous sodium hydroxide solution or by adding if necessary;
    ii. optionally filtering the clear solution obtained in step (i);
    iii. adding the solvent in which the Pantoprazole sodium is insoluble, accompanied by optionally cooling the mass to –10 to +20^{O}C and accompanied by stirring till the compound substantially crystallizes;
    iv. filtering the crystallized solid in step (iii) by conventional methods;
    v. drying of the solid obtained in step (iv) at a temperature of 40-90°C, preferably 40-50^{O}C under vacuum to a constant weight to afford the desired crystalline Form-I of Pantoprazole sodium sesqui hydrate.
2. The process according to claim (1) of step (1), wherein the solvents are selected from a group comprising of C1-C4 straight or branched alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, secondary butanol or tertiary butanol or tetrahydrofuran or acetonitrile or ethylacetate.
3. The process according to claim (2), wherein the solvent is tetrahydrofuran.
4. The process according to claim (1) of step (3), wherein the solvents are selected from a group comprising of aliphatic or alicyclic hydrocarbon solvents such as petroleum ether, hexane, n-heptane, cyclohexane or cyclo heptane or chlorinated solvents such as dichloromethane or chloroform or ethers having C1-C4 carbon

atoms in straight or branched chain such as dimethyl ether, diethyl ether, di isopropyl ether, di butyl ether, methyl ethyl ether or methyl tertiary butyl ether.

5. The process according to claim (4), wherein the solvent is dichloromethane.
6. The process according to claim (4), wherein the solvent is di isopropyl ether.
7. The process according to claim (4), wherein the solvent is methyl tertiary butyl ether.
8. The improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesqui hydrate is substantially as herein described and exemplified.

Dated 30th the day of August, 2002

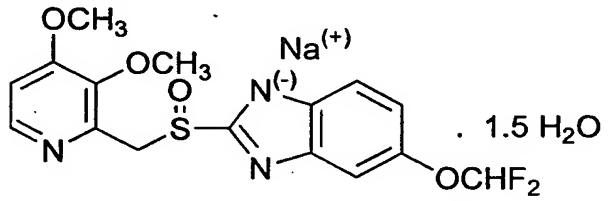
Signed)_____

Dr. Manne Satyanarayana Reddy,
Vice President (R&D),
Dr. Reddy's Laboratories Limited.

ABSTRACT

Title of the Invention: "An improved process for preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate"

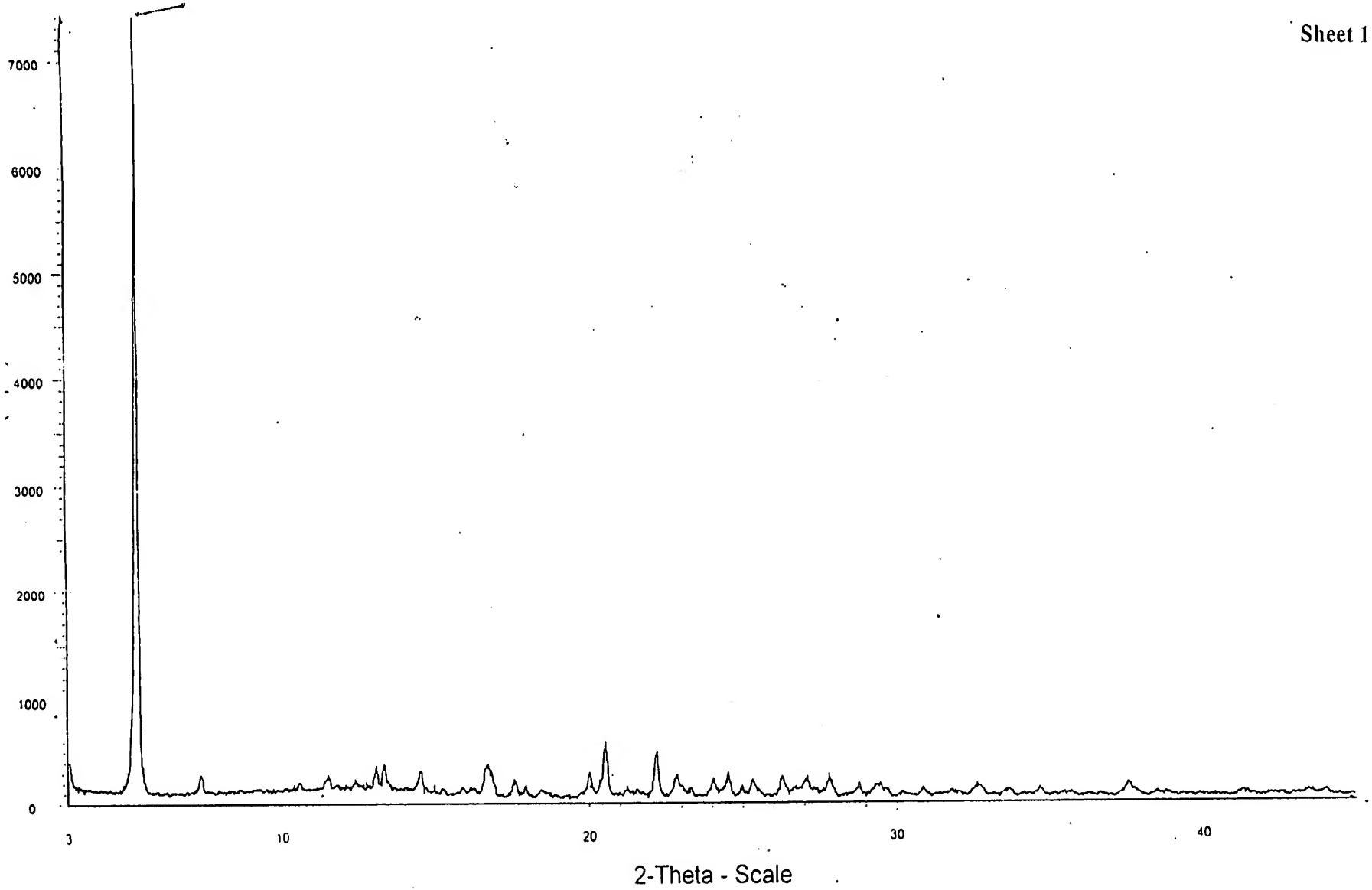
The present invention relates to an improved process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate, chemically known as 5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl) methyl] sulfinyl]-1H-benzimidazole sodium sesquihydrate. The Pantoprazole sodium sesquihydrate of the present invention can be depicted as Formula (1).



Formula (1)

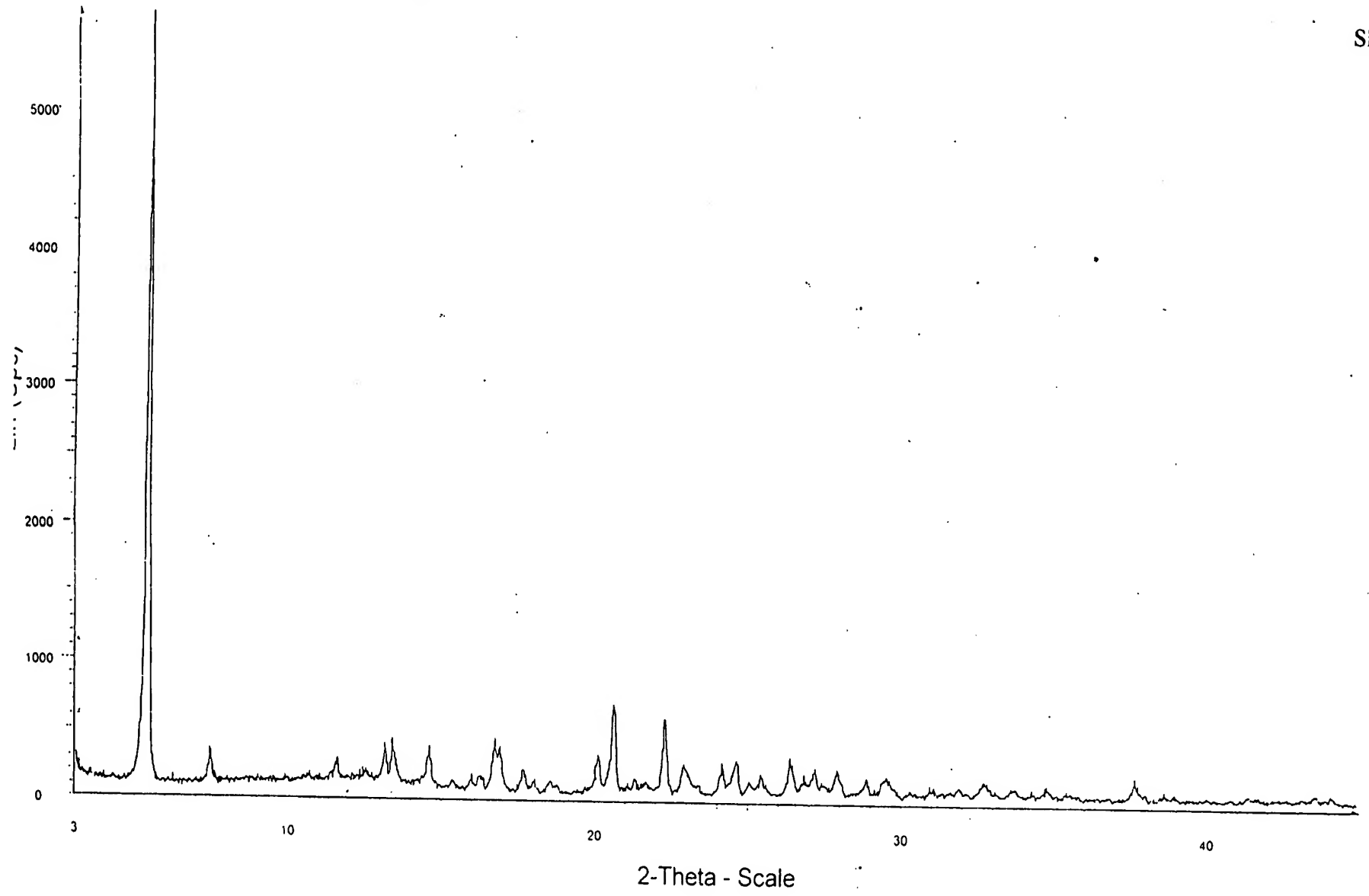
The process for the preparation of crystalline Form-I of Pantoprazole sodium sesquihydrate comprises dissolution of Pantoprazole free base in which it substantially dissolves at an ambient temperature containing a stoichiometric quantity of sodium hydroxide, filtration of the clear solution and followed by addition of anti-solvent in which the product is insoluble to isolate the desired crystalline compound.

The process of the present invention is cost effective and eco-friendly over prior art procedures.



MANNE SATYANARAYANA REDDY

Fig. 1



MANNE SATYANARAYANA REDDY

Fig.2